REMARKS

Claims 17-23, drawn to diagnostic hearing loss microarrays and kits, are pending in the present application. The claims currently stand rejected under 35 U.S.C. §102 and/or 35 U.S.C. §103 as discussed below. New claim 24 is added to claim a microarray that further comprises the genetic sequence for GJB2. Support for this claim is found, for example, in Table 1, Table 3, Paragraph [0082] and Example 5 of the specification. No new matter is added by this amendment.

Claim Rejections Under 35 U.S.C. §102

The Examiner rejected claims 17-20 under 35 U.S.C. §102(b) as being anticipated by Affymetrix catalog (2002 edition). The Examiner asserted that the HG-U133 Plus 2.0 Array contains all five genes, namely, CDH23, MYO7A, OTOF, SLC26A4 and USH2A, as well as multiple adjacent exons as recited in the instant claims. Applicants respectfully disagree with the rejection as discussed below.

According to 37 C.F.R. §1.104(d)(1), if printed publications are cited, the author (if any), title, date, pages or plates, and place of publication, or place where a copy can be found, will be given. Furthermore, copies of documents cited will be provided as set forth in MPEP §707.05(a). See MPEP §707.05 and §707.05(a). Copies of cited foreign patent documents and non-patent literature references are automatically furnished without charge to applicant together with the Office action in which they are cited.

The Examiner has cited Affymetrix catalog (2002 edition) as a §102(b) reference against claims 17-20. However, a copy of the primary reference has not been provided according to 37 C.F.R. §1.104(d)(1) for Applicants' review. Instead, a secondary reference referring to the HG-U133 Plus 2.0 Array has been provided with the Office Action. The secondary reference discloses the starting date on which orders for the HG-U133 Plus 2.0 Array were accepted, but it does not teach or suggest a diagnostic hearing loss microarray comprising the genes or multiple adjacent exons as claimed. In addition to this deficiency, the date of the secondary reference is October 2, 2003, which is less than one year before the filing date of the instant application. The secondary reference itself is therefore not a proper §102(b) reference.

The secondary reference does not provide any description of the primary reference, which is Affymetrix catalog (2002 edition). Applicants are not able to address the propriety of the cited

reference without reviewing the reference itself, which the Examiner failed to provide according to 37 C.F.R. §1.104(d)(1).

Therefore, in view of the foregoing remarks, Applicants respectfully request that the rejection be withdrawn.

Claim Rejections Under 35 U.S.C. §103

Claims 17-23 were rejected under 35 U.S.C. §103(a) as being unpatentable over Williamson et al. (Williamson, R., Curator, Deafness Gene Mutation Database, URL: http://hearing.harvard.edu/db/genelist.htm, last updated September 18, 2002) in view of Guo et al. (Guo et al. 2002. *Genome Res.* 12:447-457). The Examiner alleged that it would have been *prima facie* obvious to one of ordinary skill in the art to detect SNPs relevant to a human hearing loss associated with genes and mutations taught by Williamson by adapting the simultaneous detection of such SNPs in an exon specific array format as taught by Guo. Applicants respectfully disagree with the Examiner and submit that the claims are patentable over the cited art as discussed below.

Under section 103, the Patent and Trademark Office has the burden to establish a *prima facie* case of obviousness. *In re Piasecki*, 745 F.2d 1468, 1471-72, 223 USPQ 785, 787-87 (Fed. Cir. 1984). To establish a *prima facie* case of obviousness, three basic criteria must be met: first, the prior art reference (or references when combined) must teach or suggest all the claim limitations; second, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; finally, there must be a reasonable expectation of success. *See* M.P.E.P. § 2143. Furthermore, in meeting the burden, the Patent and Trademark Office must produce detailed evidence and is forbidden from relying on "common sense" of the skilled artisan to suggest an invalidating combination of references. *In re Lee*, 61 U.S.P.Q.2d 1430 (Fed. Cir. 2002).

The Federal Circuit has ruled that "[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." *In re Fritch* at 1784. In order to avoid using Applicants' disclosure as a blueprint to pick and choose certain elements, while ignoring others, the Examiner must supply a clear and particular motivation or suggestion to do so. The need for a clear and particular motivation is even stronger

when a selected element is only mentioned and taught as peripheral to the method of focus. Otherwise, the Examiner's true motivation is forbidden hindsight. Applicants assert that the Examiner has relied on the Applicant's disclosure for the combination of Williamson and Guo. Williamson teaches a generic list of mutations in genes related to hearing loss. However, there is no teaching or suggestion of a diagnostic hearing loss microarray or kit comprising the sequences as claimed. Without the benefit of Applicants' disclosure, there would be no reason for one of skill in the art to combine the teachings relating hearing loss gene mutations in Williamson with the unrelated teachings of a microarray directed for high-throughput SNPs analysis of MHC Class I genes in Guo. Guo is focused upon identification of SNPs related to MHC Class I genes for genetic variation analysis and population/epidemiology studies. Furthermore, there is no teaching or suggestion in Guo to define a disease phenotype based on these benign polymorphisms. Therefore, the Examiner has not provided clear and particular evidence that there is motivation to combine Williamson with Guo for a **diagnostic** hearing loss microarray or kit comprising the sequences as claimed.

Furthermore, even if there were some suggestion to combine the isolated disclosures, there would not be any reasonable expectation of success produced by the combination. The list of hearing loss mutations in Williamson provides no prioritization to the importance or prevalence of these mutations or genes in a population. One of ordinary skill in the art would not know, based on the generic list of genes provided in Williamson, to pick the specific genes and adjacent exons as claimed. Guo is silent as to any hearing loss gene, mutation or SNP. The combination of Williamson and Guo would require an undue amount of experimentation to select genes that would render a microarray or kit effective as a diagnostic hearing loss device. Therefore, one of skill in the art would not expect any degree of success for a diagnostic hearing loss microarray as claimed, based on the scant information provided by the combination of cited references.

In view of the arguments presented above, Applicants submit that a *prima facie* case of obviousness has not been made and respectfully request withdrawal of the rejection.

Conclusion

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, arguments in support of the patentability of the pending

claim set are presented above. In view of the foregoing remarks, Applicants respectfully submit that this application is in condition for allowance and request the same. If any issues remain, the Examiner is cordially invited to contact the undersigned in order to resolve such issues promptly.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: 20 Feb 2007

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